At page 22 please delete the paragraph beginning at line 13 and replace with the following:

A2

Nr-CAM is a gene identified by the method of the invention, that is expressed at high levels in glioblastoma multiforme tissue as well as certain others forms of tumors and cancers.

At page 24 please delete the paragraph beginning at line 23 and replace with the following:

A3

The present invention relates to a novel role of *Nr-CAM* in the promotion of cell transformation and tumorigenesis. In particular, the present invention relates to the Applicants' findings that (a) *Nr-CAM* is highly over-expressed in glioblastoma multiforme tumor tissue and is over-expressed in a number of other primary tumors; and (b) over-expression of *Nr-CAM* in the anti-sense orientation results in decreased cellular proliferation and colony formation of glioblastoma cells in soft agar.

At page 35, please delete the portion of the paragraph beginning at line 15 and replace with the following:

A4

The identified and isolated gene can then be inserted into an appropriate cloning vector. A large number of vector-host systems known in the art may be used. Possible vectors include, but are not limited to, plasmids or modified viruses, but the vector system must be compatible with the host cell used. Such vectors include, but are not limited to, bacteriophages such as lambda derivatives, or plasmids such as pBR322 or pUC plasmid derivatives or the Bluescript vector (Stratagene). The insertion into a cloning vectorcan, for example, can be accomplished by ligating the DNA fragment into a cloning vector, which has complementarycohesive termini. However, if the complementary restriction sites used to fragment the DNA are not present in the cloning vector, the ends of the DNA molecules may be enzymatically modified. Alternatively, any site desired may be produced by ligating nucleotide sequences (linkers) onto the DNA termini; these ligated linkers may comprise specific chemically synthesized oligonucleotides encoding restriction endonuclease recognition sequences. In an alternative method, the cleaved vector and *Nr-CAM* gene may be modified by

A4

homopolymeric tailing. Recombinant molecules can be introduced into host cells via transformation, transfection, infection, electroporation, *etc.*, so that many copies of the gene sequence are generated.

At page 105, please delete the paragraph beginning at line 20 and insert the following:

A5

As shown in Figures 8 (A and B), *hNr-CAM* was expressed at high levels in melanoma G361, lymphoblastic leukemia (MOLT-4) and Burkitt's lymphoma Raji cell lines. A low level of *hNr-CAM* expression was observed in promyelocytic leukemia (HL-60), HeLa cell S3, chronic myelogenous leukemia (K-562), colorectal adenocarcinoma (SW480) and lung carcinoma (A549). All of the cell lines studied herein expressed *hNr-CAM* mRNAs that are 1.4 kb as compared to the 7.5 kb transcript expressed in normal brain (Figure 5 (A and B)). HeLa cells S3 express low levels of both transcripts. Melanoma G361 express high levels of the 7.5 kb and low levels of the 1.4 kb transcript, suggesting alternative splicing of *hNr-CAM* mRNA during tumorigenesis.

At page 109, please delete the paragraph beginning at line 6 and insert the following:

A6

To obtain antisense "*Nr-CAM* 1/3 clone", *Nr-CAM* 1/3 (corresponding to nucleotides beginning at nucleotide 119 and ending at nucleotide 1434 of Figure 2A) was amplified using primers BT306 (5' TAGATACAACTAGTCTAATGCAGCTTAAAATA ATGCC 3')(SEQ. ID. No.: 18) and BT307 (5' AGATAGATCCGCGGATATCCATATT CATTAGAGGCATTG 3') (SEQ. ID. NO.: 19) (see Figure 2A) and cloned into precut pCMVneo vector cut with SacII and SpeI restriction enzymes. PCR amplification was carried out for 1 cycle at 94°C 3 min, 61°C 1 min, 72°C 4 min, then for 30 cycles at 94°C 1 min, 61°C 1 min, 72°C 4 min followed by 1 cycle at 94°C 1 min, 61°C 1 min, 72°C 10 min. The PCR product was cut with SpeI and SacII, and cloned in the antisense direction into the pCMVneo vector precut with SacII and SpeI enzymes. Orientation of the *hNr-CAM* gene was confirmed by restriction digestion of specific enzymes. This clone was termed "pCMV-1/3Nr-AS".

At page 122, please delete the paragraph beginning at line 25 and insert the following:

The effect of ODNs on inhibition of *hNr-CAM* expression can be evaluated using the methodology described previously (Anfossi, *et al.*, 1989 *Proc Natl Acad Sci USA*, 86:3379-3383). Briefly, 5GB, HTB-16 and GB1690 cells are plated per well in 96-well plates in media without ODNs. Twenty-four hours later, the culture media is changed to contain a final concentration of 1mmole/L, 3mmole/L, or 10mmole/L ODNs. Control cultures received fresh culture media without ODNs. After 4-5 days post-transfection, cell proliferation is analyzed using a cell proliferation assay kit from Promega (Madison, WI). Expression is analyzed using immunocytochemistry methods, described previously (Sehgal, *et al.*, 1998, *Int. J. Cancer*, 76(4):451-458). These oligonucleotides are tagged with fluorescent tags to ensure their entry into the cells.

A7

At page 124, please delete the paragraph beginning at line 11 and insert the following:

As a non-limiting, illustrative example the following is presented. A Retro-X™ system is used to deliver and over-express antisense *hNr-CAM* gene in glioblastoma cells. Retro-X™ system is a complete retroviral gene expression system that can transduce up to 100% of cells. Together with the RetroPack™, PT67 cell line, the Retro-X Vectors produce infectious, replication-incompetent retrovirus that can be used to introduce a gene of interest into a wide variety of mammalian cell types *in vitro* or *in vivo*. The highly efficient transduction machinery of retroviruses can stably integrate the cloned gene into the host genome of nearly all mitotically dividing cells. A retroviral vector containing the gene of interest (*hNr-CAM*) is first transfected into the packaging cell line. Antibiotic selection can then be used to obtain a population of cells that satably expresses the integrated vector and, if desired, high-titer clones can be isolated from this population. Virus produced by either stably transfected cells can be used to infect target cells.

A8

At page 126, please delete the paragraph beginning at line 13 and insert the following:

Northern blot analysis for the expression of *hNr-CAM*. Cell clones that are expressing low level of *hNr-CAM* are expanded in culture. Approximately $1x10^7$ glioblastoma cells (1690-CRL, 1620-CRL, HTB-16, C6, 9L gliosarcoma) will be injected subcutaneously into the flanks of ten female athymic nude mice (two sites each). Tumor growth will be analyzed every week for at least fourteen weeks and compared between anti-sense *hNr-CAM* and mock infected glioma cell lines.

At page 129, please delete the paragraph beginning at line 14 and insert the following:

As shown in Figures 26(A and B), two genes were identified that were differentially expressed. Selectin (endothelial adhesion molecule 2) was detected in pCMV-neo transfected cells (Figure 26B) and not in pCMV-1/3Nr-AS (Figure 26A) transfected 5GB cells. A novel gene (accession # H7785) was detected in pCMV-1/3Nr-AS (Figure 26A) transfected and not in pCMV-neo transfected (Figure 26B) 5GB cells. We are not only interested in exploring the role of these genes in glioblastoma cells in the context of *hNr-CAM* over-expression but also in understanding the mechanism by which *hNr-CAM* modulates the expression of these genes.

IN THE CLAIMS:

Please cancel claims 10-12, 13, 16, 17, and 19.

Kindly replace claims 1 and 3 with the following substitute claims. An Appendix showing all changes to these claims is attached to this amendment as required by 37 CFR §1.121(c).

1. (Amended) A pharmaceutical composition for the inhibition of tumorigenesis comprising an antisense nucleic acid comprising at least 15 nucleotides hybridizable in a cell to at least a portion of an RNA transcript of a *Nr-CAM* gene of SEQ